UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460

OFFICE OF
PREVENTION, PESTICIDES
AND TOXIC SUBSTANCES

Note to Reader

Background: As part of its effort to involve the public in the implementation of the Food Quality Protection Act of 1996 (FQPA), which is designed to ensure that the United States continues to have the safest and most abundant food supply. EPA is undertaking an effort to open public dockets on the organophosphate pesticides. These dockets will make available to all interested parties documents that were developed as part of the U.S. Environmental Protection Agency's process for making reregistration eligibility decisions and tolerance reassessments consistent with FQPA. The dockets include preliminary health assessments and, where available, ecological risk assessments conducted by EPA, rebuttals or corrections to the risk assessments submitted by chemical registrants, and the Agency's response to the registrants' submissions.

The analyses contained in this docket are preliminary in nature and represent the information available to EPA at the time they were prepared. Additional information may have been submitted to EPA which has not yet been incorporated into these analyses, and registrants or others may be developing relevant information. It's common and appropriate that new information and analyses will be used to revise and refine the evaluations contained in these dockets to make them more comprehensive and realistic. The Agency cautions against premature conclusions based on these preliminary assessments and against any use of information contained in these documents out of their full context. Throughout this process, If unacceptable risks are identified, EPA will act to reduce or eliminate the risks.

There is a 60 day comment period in which the public and all interested parties are invited to submit comments on the information in this docket. Comments should directly relate to this organophosphate and to the information and issues available in the information docket. Once the comment period closes, EPA will review all comments and revise the risk assessments, as necessary.

These preliminary risk assessments represent an early stage in the process by which EPA is evaluating the regulatory requirements applicable to existing pesticides. Through this opportunity for notice and comment, the Agency hopes to advance the openness and scientific soundness underpinning its decisions. This process is designed to assure that America continues to enjoy the safest and most abundant food supply. Through implementation of EPA's tolerance reassessment program under the Food Quality Protection Act, the food supply will become even safer. Leading health experts recommend that all people eat a wide variety of foods, including at least five servings of fruits and vegetables a day.

Note: This sheet is provided to help the reader understand how refined and developed the pesticide file is as of the date prepared, what if any changes have occurred recently, and what new information, if any, is expected to be included in the analysis before decisions are made. **It is not meant to be a summary of all current information regarding the chemical.** Rather, the sheet provides some context to better understand the substantive material in the docket (RED chapters, registrant rebuttals, Agency responses to rebuttals, etc.) for this pesticide.

Further, in some cases, differences may be noted between the RED chapters and the Agency's comprehensive reports on the hazard identification information and safety factors for all organophosphates. In these cases, information in the comprehensive reports is the most current and will, barring the submission of more data that the Agency finds useful, be used in the risk assessments.

Jack E. Housenger, Acting Director
Special Review and Reregistration Division

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460

OFFICE OF
PREVENTION, PESTICIDES AND
TOXIC SUBSTANCES

May 5, 1999

MEMORANDUM

SUBJECT: OCCUPATIONAL EXPOSURE AND RISK ASSESSMENT REGARDING THE USE OF PHOSTEBUPIRIM. (PC 129086 and DP Barcode D255284)

FROM: Renee Sandvig, Environmental Protection Specialist
Reregistration Branch II
Health Effects Division (7509C)

TO: Amy Caicedo
Special Review Branch
Special Review and Reregistration Division (7508W)

THRU: Al Nielsen, Senior Scientist
Reregistration Branch II
Health Effects Division (7509C)

Please find attached a occupational exposure and risk assessment for the use of phostebupirim.

DB Barcode: D255284

Pesticide Chemical Codes: 129086

EPA Reg Nos: 3125-411, 3125-412, and 3125-513

EPA MRID No.: N/A

PHED: Yes, Version 1.1

OCCUPATIONAL EXPOSURE AND RISK ASSESSMENT FOR THE USE OF PHOSTEBUPIRIM.

In this document, which is for use in EPA's development of the Phostebupirim risk assessment, HED presents the results of its occupational exposure and risk assessment for the use of phostebupirim.

Use Patterns

Phostebupirim (O-[2-(1,1-dimethylethyl)-5-pyrimidinyl] O-ethyl O-(1-methylethyl) phosphorothioate) is an organophosphorus insecticide registered by Bayer Corporation (formerly Miles, Inc.) for the control of corn rootworms, cutworms, and other soil insect pests in corn commodities (forage and fodder, pop, and sweet). Formulations include the 93% liquid Technical (3125-411), Aztec 2.1% Granular Insecticide (3125-412), and Aztec 4.67% Granular Insecticide (3125-513). Aztec 4.67% Granular Insecticide was registered on October 22, 1998 and is for use only with a SmartBox® applicator system.[1]

Phostebupirim can be applied to corn only with tractor drawn spreader. The label maximum application rates vary from 0.11 to 0.15 pounds active ingredient per acre depending upon the application scenario.[1] Both formulations have the same application rate of the active ingredient.

Summary of Toxicity Concerns

Acute Toxicology Categories

Table 1 presents the acute toxicity categories as outlined in the HED Risk Assessment for Use of Aztec 2.1% granular on Corn Commodities, dated February 16, 1995.[2]

Table 1. Toxicity Categories.

Study Type	Toxicity Category (technical)	Toxicity Category (Aztec 4.67%)
Acute Oral Toxicity	I	II
Acute Dermal Toxicity	I	III
Acute Inhalation Toxicity	I	III
Primary Eye Irritation	Not Available	III
Primary Dermal Irritation	Not Available	IV
Dermal Sensitization	Not Available	slight

Toxicological Endpoints of Concern

The phostebupirim endpoints were obtained from the HED Risk Assessment for Use of Aztec 2.1% Granular on Corn Commodities, dated February 16, 1995 and they indicate that there are toxicological endpoints of concern for phostebupirim. Dermal and inhalation endpoints of concern have been identified for short-term and intermediate-term exposures.[2]

The toxicity endpoints selected for risk assessment are based primarily on plasma, red blood cell, and brain cholinesterase inhibition. Phostebupirim is classified as a Group E chemical, indicating that it is "Not Likely" to be carcinogenic in humans via relevant routes of exposure. This classification is supported by adequate carcinogenicity studies in rats and mice.[2]

On December 3, 1998, the HIARC met to re-evaluate the dermal absorption factors used for 16 organophosphates. For phostebupirim, the Committee determined that a dermal absorption value of 100% is appropriate since comparison of the 21-day dermal toxicity study and the oral developmental toxicity study (both in rabbits) indicates high toxicity by both routes at very dose levels (1 mg/kg/day or less).[3]

Table 2. Phostebupirim Hazard Endpoints and Uncertainty Factors.

Route / Duration	NOAEL (mg/kg/day)	Effect	Study	Uncertainty Factors	Comments
Dermal short term	0.1	Increased Number of Fetal Resorptions	developmental toxicity in rabbits.	Interspecies: 10x Intraspecies: 10x	100 percent dermal assumed.
Dermal intermediate term	0.02	Red Blood Cell Cholinesterase Inhibition	1-year chronic dog study	Interspecies: 10x Intraspecies: 10x	100 percent dermal assumed.
Inhalation (short and intermediate term)	0.043 (0.16 mg/m^3)[a]	Red Blood Cell Cholinesterase Inhibition	28 day inhalation study in rats.	Interspecies: 10x Intraspecies: 10x	Wistar Rats, 6 hrs/day exposure, 100 percent lung absorption assumed.

a 0.16 mg/m^3 was converted to 0.043 mg/kg/day by the following formula: NOAEL (mg/kg/day) = NOAEL (mg/m^3) * Conversion Factor (1m^3 / 1000 L) * Wistar Rat Respiratory Volume for Males and Females (8.46 L/hr) * Body Weight of Wistar Rats for Males and Females (1/0.187 kg) * Exposure Duration per day (6 hrs/day).[4]

The short term dermal and inhalation NOAELs were not based on identical effects; therefore, the MOEs were not combined in this risk assessment. The intermediate term dermal and inhalation NOAELs were based on identical endpoints, the MOEs were combined to identify a total MOE. Since a developmental study was used to determine the short term dermal NOAEL, the body weight used to calculate short term dermal dose was 60 kg, the average weight of an adult female. No chronic scenarios were identified.

OCCUPATIONAL EXPOSURE AND RISKS

Chemical-specific data for assessing human exposures during pesticide handling activities were not submitted to the Agency in support of the reregistration of phostebupirim. It is the policy of the HED to use data from the Pesticide Handlers Exposure Database (PHED) Version 1.1 to assess handler exposures for regulatory actions when chemical-specific monitoring data are not available.[5]

PHED was designed by a task force of representatives from the U.S. EPA, Health Canada, the California Department of Pesticide regulation, and member companies of the American Crop Protection Association. PHED is a software system consisting of two parts -- a database of measured exposure values for workers involved in the handling of pesticides under actual field conditions and a set of computer algorithms used to subset and statistically summarize the selected data. Currently, the database contains values for over 1,700 monitored individuals (i.e., replicates)

Users select criteria to subset the PHED database to reflect the exposure scenario being evaluated. The subsetting algorithms in PHED are based on the central assumption that the magnitude of handler exposures to pesticides are primarily a function of activity (i.e. mixing/loading, applying), formulation type (i.e. granulars), application method (i.e., tractor drawn spreader), and clothing scenarios (i.e., gloves, double layer clothing).

Once the data for a given exposure scenario have been selected, the data are normalized (i.e., divided by) by the amount of pesticide handled resulting in standard unit exposures (milligrams of exposure per pound of active ingredient handled). Following normalization, the data are statistically summarized. The distribution of exposure values for each body part (i.e., chest upper arm) is categorized as normal, lognormal, or "other" (i.e., neither normal nor lognormal). A central tendency value is then selected from the distribution of the exposure values for each body part. These values are the arithmetic mean for normal distributions, the geometric mean for lognormal distributions, and the median for all "other" distributions. Once selected, the central tendency values for each body part are composited into a "best fit" exposure value representing the entire body.

The unit exposure values calculated by PHED generally range from the geometric mean to the median of the selected data set. To add consistency and quality control to the values produced from this system, the PHED Task Force has evaluated all data within the system and has developed a set of grading criteria to characterize the quality of the original study data. The assessment of data quality is based on the number of observations and the available quality control data. These evaluation criteria and the caveats specific to each exposure scenario are summarized in Table 6. While data from PHED provide the best available information on handler exposures, it should be noted that some aspects of the included studies (e.g., duration, acres treated, pounds of active ingredient handled) may not accurately represent labeled uses in all cases. HED has developed a series of tables of standard unit exposure values for many occupational scenarios that can be utilized to ensure consistency in exposure assessments.[6]

Handler Exposures & Assumptions

HED has determined that there are potential exposures to mixers, loaders, applicators, and other handlers during usual use-patterns associated with phostebupirim. Based on the use patterns of phostebupirim, four major exposure scenarios were identified: (1a) loading granulars at a typical acreage; (1a) loading granulars at a maximum acreage; (2a) applying granulars with a tractor drawn spreader at a typical acreage; (2b) applying granulars with a tractor drawn spreader at a maximum acreage.

Short-term and intermediate-term exposures and doses at baseline (developed using PHED Version 1.1 surrogate data) are presented in Table 3. The short- and intermediate-term MOEs with mitigation methods to handlers are presented in Table 4 and Table 5. The short and intermediate-term inhalation MOEs are identical since they have the same endpoint. Table 6 summarizes the caveats and parameters specific to each exposure scenario and corresponding risk assessment.

The following general assumptions are made:

- Average body weight of an adult handler is 70 kg. An average body weight of 60 kg was used for an adult female for short-term dermal exposure since the NOAEL is based on a reproductive study. Since the dermal and inhalation NOAELs for the short and intermediate-term were not based on identical endpoints, the doses were not combined in this risk assessment to identify a total MOE.

- Average work day interval represents an 8 hour workday (e.g., the acres treated or volume of spray solution prepared in a typical day).

- Calculations of handler scenarios are completed using the application rates recommended by the available phostebupirim.

- PHED Version 1.1 data were used for to estimate exposures for all scenarios.[6]

- Due to a lack of scenario-specific data, HED calculated unit exposure values using generic data from the Pesticide Handler Exposure Database (PHED) and, in lieu of PHED data for a scenario, using protection factors that are applied to represent various risk mitigation options (i.e., the use of PPE and engineering controls). See Table 6 for details.

- Exposures were estimated for handlers using 213 acres per day maximum acreage (20 row planter) and 69 acres per day typical acreage (8 row planter) for a tractor drawn spreader at the minimum and maximum application rates, since these data were available from the Corn Insecticide Cluster Risk Assessment for Occupational Exposure (BEAD supplied data).[7]

Potential daily dermal exposure is calculated using the following formula:

$$\text{Daily Dermal Exposure}\left(\frac{mg\ ai}{day}\right) = \text{Unit Exposure}\left(\frac{mg\ ai}{lb\ ai}\right) \times \text{Use Rate}\left(\frac{lb\ ai}{A}\right) \times \text{Daily Acres Treated}\left(\frac{A}{day}\right)$$

A 100 percent dermal absorption value is assumed.

Potential daily inhalation exposure is calculated using the following formula:

$$\text{Daily Inhalation Exposure}\left(\frac{mg\ ai}{day}\right) =$$
$$\text{Unit Exposure}\left(\frac{\mu g\ ai}{lb\ ai}\right) \times \text{Conversion Factor}\left(\frac{1mg}{1{,}000\ \mu g}\right) \times \text{Use Rate}\left(\frac{lb\ ai}{A}\right) \times \text{Daily Acres Treated}\left(\frac{A}{day}\right)$$

The daily dermal and inhalation dose is calculated using a 70 kg body weight for both short-term and intermediate-term exposure as follows:

$$\text{Daily Inhalation Dose}\left(\frac{mg\ ai}{kg/day}\right) = \text{Daily Inhalation Exposure}\left(\frac{mg\ ai}{day}\right) \times \left(\frac{1}{\text{Body Weight (kg)}}\right)$$

$$\text{Daily Dermal Dose}\left(\frac{mg\ ai}{Kg/Day}\right) = \text{Daily Dermal Exposure}\left(\frac{mg\ ai}{Day}\right) \times \left(\frac{1}{\text{Body Weight (Kg)}}\right)$$

Based on the available toxicity data, it is not appropriate to combine short-term dermal and inhalation MOEs because the effects observed at the NOAEL are different. It is necessary to combine the intermediate-term dermal and inhalation MOEs, since the effect observed at the NOAEL were identical. The short-term and intermediate-term total MOE for dermal exposure were calculated using a NOAEL of 0.1 mg/kg/day and a NOAEL of 0.02 mg/kg/day, respectively. Both the short-term and intermediate-term total MOE for inhalation exposure were calculated using a NOAEL of 0.16 mg/m^3 which translates to 0.043 mg/kg/day[4] by the following formula:

$$\text{NOAEL}\left(\frac{mg}{kg/day}\right) = \text{NOAEL}\left(\frac{mg}{m^3}\right) \times \text{Conversion Factor}\left(\frac{1\ m^3}{1000\ L}\right)$$
$$\times \text{Wistar Rat Respiratory Volumes}\left(\frac{8.46\ L}{hr}\right)$$
$$\times \text{Body Weight of Wistar Rat}\left(\frac{1}{0.187\ kg}\right) \times \text{Exposure Duration}\left(\frac{6\ hrs}{day}\right)$$

The inhalation and dermal MOEs were calculated using the following formulas:

$$Dermal\ MOE = \frac{NOAEL\left(\frac{mg}{kg/day}\right)}{Dermal\ Daily\ Dose\left(\frac{mg}{kg/day}\right)}$$

$$Inhalation\ MOE = \frac{NOAEL\left(\frac{mg}{kg/day}\right)}{Inhalation\ Daily\ Dose\left(\frac{mg}{kg/day}\right)}$$

The total intermediate-term MOE were calculated using the following formula:

$$Total\ Intermediate\ term\ MOE = \frac{1}{\left(\frac{1}{intermediate\ term\ dermal\ MOE}\right) + \left(\frac{1}{intermediate\ term\ inhalation\ MOE}\right)}$$

Table 3. Occupational Short-Term and Intermediate-Term Dermal and Inhalation Exposure to Phostebupirim and Doses at Baseline.

Exposure Scenario (Scenario #)	Baseline Dermal Unit Exposure (mg/lb ai)[a]	Baseline Inhalation Unit Exposure (μg/lb ai)[b]	Application Rate (lb ai/acre)[c]	Rate	Daily Acres Treated[d]	Daily Dermal Exposure (mg/day)[e]	Daily Inhalation Exposure (mg/day)[f]	Baseline Short-term Dermal Dose (mg/kg/day)[g]	Baseline Int.- term Dermal Dose (mg/kg/day)[h]	Baseline Inhalation Dose (mg/kg/ day)[i]	Short-term Dermal MOE[j]	Int.-term Dermal MOE[k]	Short- and Int.- term Inhalation MOE[l]	Total Int.-term MOE[m]
Loader Exposure and Dose Levels														
Loading Granules at a Typical Acreage (1a)	0.0084	1.7	0.11	minimum	69	0.064	0.013	0.0011	0.00091	0.00018	94	22	230	20
			0.15	maximum		0.087	0.018	0.0015	0.0012	0.00025	69	16	170	15
Loading Granules at the Maximum Acreage(1b)			0.11	minimum	213	0.20	0.040	0.0033	0.0028	0.00057	30	7	76	7
			0.15	maximum		0.27	0.054	0.0045	0.0038	0.00078	22	5	55	5
Applicator Exposure and Dose Levels														
Applying Granules with a Tractor Drawn Spreader at a Typical Acreage (2a)	0.0099	1.2	0.11	minimum	69	0.075	0.0091	0.0013	0.0011	0.00013	80	19	330	18
			0.15	maximum		0.10	0.012	0.0017	0.0015	0.00018	59	14	240	13
Applying Granules with a Tractor Drawn Spreader at the Maximum Acreage (2b)			0.11	minimum	213	0.23	0.028	0.0039	0.0033	0.00040	26	6	110	6
			0.15	maximum		0.32	0.038	0.0053	0.0045	0.00055	19	4	79	4

Footnotes

a Baseline dermal unit exposure represents long pants, long sleeved shirt, no gloves, open mixing/loading, open cab tractor.
b Baseline inhalation exposure represents no respirator.
c Application rates are a range of application rates from the labels.
d Acres treated are based on 8 row planters (69 acres/day) (typical acreage) and 20 row planters (213 acres/day) (maximum acreage).
e Daily dermal exposure (mg/day) = Dermal Unit Exposure (mg/lb ai) * Application rate (lb ai/acre) * Acres treated (acres/day).
f Daily inhalation exposure (mg/day) = Inhalation Unit Exposure (µg/lb ai) * (1mg/1000 µg) Conversion factor * Application rate (lb ai/A) * Acres treated (acres/day).
g Short- term Baseline dermal dose (mg/kg/day) = Daily dermal exposure / Body weight (60 kg).
h Intermediate-term Baseline dermal dose (mg/kg/day) = Daily dermal exposure / Body weight (70 kg).
i Baseline inhalation dose (mg/kg/day) = Daily inhalation exposure / Body weight (70 kg).
j Short-term Dermal MOE = Short term Dermal NOAEL (0.1 mg/kg/day)/Short Term Dermal Dose (mg/kg/day).
k Intermediate-term Dermal MOE = Intermediate term Dermal NOAEL (0.02 mg/kg/day)/Intermediate term Dermal Dose (mg/kg/day).
l Short- and Intermediate-term Inhalation MOE = Short and Intermediate term Inhalation NOAEL (0.043 mg/kg/day)/ Daily Inhalation Dose (mg/kg/day).
m Total Intermediate-term MOE = 1/((1/Intermediate-term Dermal MOE) + (1/Intermediate-term Inhalation MOE)).

Table 4. Occupational Short-Term and Intermediate-Term Dermal and Inhalation Exposure to Phostebupirim and Doses at Additional PPE.

Exposure Scenario (Scenario #)	Rate	Additional PPE								
		Unit Dermal Exposure[a] (mg/lb ai)	Short-term Dermal Dose[b] (mg/kg/day)	Int.- term Dermal Dose[c] (mg/kg/day)	Unit Inhalation Exposure[d] (mg/lb ai)	Daily Inhalation Dose[e] (mg/kg/day)	Short-term Dermal MOE[f]	Int.- term Dermal MOE[g]	Short- and Int.- term Inhalation MOE[h]	Total Int.- term MOE[i]
Loader Exposure and Dose Levels										
Loading Granules at a Typical Acreage (1a)	Minimum	0.0034	0.00043	0.00037	0.34	0.00004	230	54	1200	52
	Maximum		0.00059	0.00050		0.00005	170	40	860	38
Loading Granules at the Maximum Acreage (1b)	Minimum		0.0013	0.0011		0.00011	75	18	380	17
	Maximum		0.0018	0.0016		0.00016	55	13	280	12
Applicator Exposure and Dose Levels										
Applying Granules with a Tractor Drawn Spreader at a Typical Acreage (2a)	Minimum	0.0042	0.00053	0.00046	0.24	0.00003	190	44	1700	43
	Maximum		0.00072	0.00062		0.00004	140	32	1200	31
Applying Granules with a Tractor Drawn Spreader at the Maximum Acreage (2b)	Minimum		0.0016	0.0014		0.00008	61	14	540	14
	Maximum		0.0022	0.0019		0.00011	45	10	390	10

Footnotes

a Additional PPE for all dermal scenarios includes double layer of clothing (50% Protection Factor for clothing) and chemical resistant gloves (90% Protection Factor).
b Short- term Daily Dermal Dose (mg/kg/day) = ((Dermal Unit Exposure (mg/lb ai) x Application Rates (lb ai/A and lb ai/sq. ft.) x Area Treated per day (acres)) / Body Weight (60 kg))
c Intermediate-term Daily Dermal Dose (mg/kg/day) = ((Dermal Unit Exposure (mg/lb ai) x Application Rates (lb ai/A and lb ai/sq. ft.) x Area Treated per day (acres)) / Body Weight (70 kg))
d Additional PPE for all inhalation scenarios includes a dust/mist respirator (80% protection factor).
e Daily Inhalation Dose = ((Inhalation Unit Exposure (mg/lb ai) x Application Rates (lb ai/A and lb ai/sq. ft.) x Area Treated per day (acres)) / Body Weight (70 kg))
f Short term Dermal MOE = Short term Dermal NOAEL (0.1 mg/kg/day)/ Short Term Dermal Dose (mg/kg/day).
g Intermediate- term Dermal MOE = Intermediate term Dermal NOAEL (0.02 mg/kg/day)/ Intermediate Term Dermal Dose (mg/kg/day).
h Short- and Intermediate-term Inhalation MOE = Short and Intermediate term Inhalation NOAEL (0.043 mg/kg/day)/ Daily Inhalation Dose (mg/kg/day).
i Total Intermediate-Term MOE = 1/((1/dermal intermediate-term MOE) + (1/inhalation intermediate-term MOE))

Table 5. Occupational Short-Term and Intermediate-Term Dermal and Inhalation Exposure to Phostebupirim and Doses with Engineering Controls.

Exposure Scenario (Scenario #)	Rate	Engineering Controls								
		Unit Dermal Exposure[a] (mg/lb ai)	Short-term Dermal Dose[b] (mg/kg/day)	Int.- term Dermal Dose[c] (mg/kg/day)	Unit Inhalation Exposure[a] (mg/lb ai)	Daily Inhalation Dose[d] (mg/kg/day)	Short term Dermal MOE[e]	Int.- term Dermal MOE[f]	Short- and Int.-term Inhalation MOE[g]	Total Int.-term MOE[h]
Loader Exposure and Dose Levels										
Loading Granules at a Typical Acreage (1a)	Minimum	0.00017	0.000022	0.000018	0.034	0.0000037	4700	1100	12000	990
	Maximum		0.000029	0.000025		0.0000050	3400	800	8600	730
Loading Granules at the Maximum Acreage (1b)	Minimum		0.000066	0.000057		0.000011	1500	350	3800	320
	Maximum		0.000091	0.000078		0.000016	1100	260	2800	240
Applicator Exposure and Dose Levels										
Applying Granules with a Tractor Drawn Spreader at a Typical Acreage (2a)	Minimum	0.0021	0.00027	0.00023	0.22	0.000024	380	88	1800	84
	Maximum		0.00036	0.00031		0.000033	280	64	1300	61
Applying Granules with a Tractor Drawn Spreader at the Maximum Acreage (2b)	Minimum		0.00082	0.00070		0.000074	120	28	580	27
	Maximum		0.0011	0.00096		0.00010	89	21	430	20

Footnotes

a Scenario Number — Engineering Controls
1a / 1b — Closed mixing / loading (e.g. Lock and Load® or Smart Boxes® 98% protection factor), single layer clothing, chemical resistant gloves.
2a/2b — Enclosed cab, single layer clothing, no gloves.(98% protection factor)

b Short-term Dermal Dose (mg/kg/day) = ((Dermal Unit Exposure (mg/lb ai) x Application Rates (lb ai/A and lb ai/sq. ft.) x Area Treated per day (acres)) / Body Weight (60 kg))
c Intermediate-term Dermal Dose (mg/kg/day) = ((Dermal Unit Exposure (mg/lb ai) x Application Rates (lb ai/A and lb ai/sq. ft.) x Area Treated per day (acres)) / Body Weight (70 kg))
d Daily Inhalation Dose = ((Inhalation Unit Exposure (mg/lb ai) x Application Rates (lb ai/A and lb ai/sq. ft.) x Area Treated per day (acres)) / Body Weight (70 kg))
e Short-term Dermal MOE = Short term Dermal NOAEL (0.1 mg/kg/day)/ Short Term Dermal Dose (mg/kg/day).
f Intermediate- term Dermal MOE = Intermediate term Dermal NOAEL (0.02 mg/kg/day)/ Intermediate Term Dermal Dose (mg/kg/day).
g Short- and Intermediate-term Inhalation MOE = Short- and Intermediate- term Inhalation NOAEL (0.043 mg/kg/day)/ Daily Inhalation Dose (mg/kg/day).
h Total Intermediate-term MOE = 1/((1/dermal intermediate-term MOE) + (1/inhalation intermediate-term MOE)).

Table 6. Occupational Exposure Scenario Descriptions for the Use of Phostebupirim

Exposure Scenario (Number)	Data Source	Standard Assumptions[a] (8-hr work day)	Comments[b]
Loader Exposure			
Loading granules for tractor drawn/ mechanical spreader application (1a/1b)	PHED V1.1	80 acres for tractor drawn spreader	**Baseline:** Hand data are All grades, and dermal and inhalation are ABC grades. Hand = 10 replicates; dermal = 33 to 78 replicates; and inhalation = 58 replicates. Low confidence in hand/dermal data, and high confidence in inhalation data. No protection factor was needed to define the unit exposure value. **PPE:** Hand data are AB grades, and dermal data are ABC grades. The same inhalation data are used as for the baseline coupled with an 80% protection factor to account for the use of a dust/mist respirator. Hand = 45 replicates and dermal = 12 to 59 replicates. Low confidence in hand/dermal data. **Engineering Controls:** Hand data are All grades; dermal are ABC grades; and inhalation are AB grades. Hand = 10 replicates; dermal =33 to 78 replicates; inhalation = 58 replicates. Low confidence in hand/dermal data and high confidence in inhalation data.
Applicator Exposure			
Applying granules with tractor-drawn spreader (2a/2b)	PHED V1.1	80 acres for tractor drawn spreader	**Baseline:** Hand, dermal, and inhalation data are AB grades. Hand = 5 replicates; dermal = 1 to 5 replicates; and inhalation = 5 replicates. Low confidence in hand/dermal and inhalation data. No protection factor was needed to define the unit exposure value. **PPE:** The same hand and dermal data are used as for the baseline coupled with a 90% protection factor to account for chemical resistant gloves, and a 50% protection factor to account for an additional layer of clothing, respectively. The same inhalation data are used as for the baseline coupled with an 80% protection factor to account for the use of a dust/mist respirator. **Engineering Controls:** Hand, dermal, and inhalation data are AB grades. Hand = 24 replicates; dermal =27 to 30 replicates; inhalation = 37 replicates. High confidence in hand/dermal and inhalation data.

Footnotes

[a] Standard Assumptions based on an 8-hour work day as estimated by EPA. BEAD data were not available.

[b] "Best Available" grades are defined by EPA SOP for meeting Subdivision U Guidelines. Acceptable grades are matrices with grades A and B data. Data confidence are assigned as follows:

High = grades A and B and 15 or more replicates
Medium = grades A, B, and C and 15 or more replicates
Low = grades A, B, C, D, and E or any combination of grades with less than 15 replicates

Summary of Risk Concerns for Occupational Handlers

The acceptable MOE for all scenarios is 100. The short-term dermal and inhalation NOAELs were not based on identical effects; therefore, the MOEs were not combined in this risk assessment. The intermediate-term dermal and inhalation NOAELs were based on identical endpoints, the MOEs were combined to identify a total intermediate-term MOE.

Baseline Level

All calculated short-term dermal MOEs were **less than** 100 at the **baseline** level.

The calculations of short-term inhalation risk indicate that inhalation MOEs are **more than** 100 at the **baseline** level for the all the assessed exposure scenarios **except** the following:

- (1b) Loading granules at the maximum acreage for both application rates.
- (2b) Applying granules at the maximum acreage for tractor drawn spreader application at the maximum application rate.

All calculated total intermediate-term MOEs were **less than** 100 at the **baseline** level.

Additional PPE

The calculations of short-term dermal risk indicate that the dermal MOEs are **more than** 100 at the **additional PPE** level for all assessed exposure scenarios **except** the following:

- (1b) Loading granules at the maximum acreage for both application rates.
- (2b) Applying granules at the maximum acreage for tractor drawn spreader application for both application rates.

All calculated short-term inhalation MOEs were **more than** 100 at the **additional PPE** level.

All calculated total intermediate-term MOEs were **less than** 100 at the **additional PPE** level.

Engineering Controls

The calculations of short-term dermal risk indicate that the MOEs are **more than** 100 at the **engineering control level** for all assessed exposure scenarios **except** the following:

- (2b) Applying granules at the maximum acreage for tractor drawn spreader application for the maximum application rate.

All calculated short-term inhalation MOEs were **more than** 100 at the **engineering control level**.

The calculations of total intermediate-term risk indicate that the MOEs are **more than** 100 at the **engineering control level** for all assessed exposure scenarios **except** the following:

- (2a) Applying granules at the typical acreage for tractor drawn spreader application for both application rates.

- (2b) Applying granules at the maximum acreage for tractor drawn spreader application for both application rates.

Post Application:

The present labels for phostebupirim state that the re-entry interval (REI) is 0 hours. This was a result of a memo, Requested Waiver of WPS Label Statements for Aztec 2.1% Granular Insecticide, dated September 13, 1994.[8] This decision was made because phostebupirim was a soil incorporated insecticide and there was no expected contact with the soil after the insecticide was incorporated.

The Worker Protection Standard for Agricultural Pesticides was issued in 1992 and includes pesticides that are applied through soil-incorporation. The Agency decided that workers do reenter treated areas after pesticides are applied through soil-incorporation and that some of those tasks would result in contact with the pesticide residues in the soil subsurface. For example, after a soil-incorporated insecticide treatment was applied while planting corn seed, workers might enter and disturb the soil subsurface to repair/install drainage tiles or ditches, to ascertain pesticide distribution/efficacy, or to determine the distribution/germination of the corn seeds. In addition, since adverse effects on workers may result from a combination of the toxicity of the pesticide and the amount of exposure, even relatively small amounts of highly toxic pesticides can cause poisoning. For these reasons, the Agency decided that a restricted-entry interval must be established for every pesticide application within the scope of the Worker Protection Standard, including applications that involve soil-incorporation.

A restricted-entry interval (REI), by definition, applies to workers who enter treated areas and contact treated surfaces. If workers will have no contact with the residues of the pesticide to which the REI applies, they can enter pesticide-treated areas without restriction after the pesticide application is finished. In the preamble to the WPS, EPA specifically lists the following as an example of a situation where a worker would not be expected to contact pesticide residues in a treated area:

> "After a pesticide application that is incorporated or injected into the soil, the worker is doing tasks that do not involve touching or disrupting the soil subsurface."

During the implementation of the WPS, registrants were encouraged to place the following statement on the labeling of pesticides with use-directions for soil-incorporation and locate it immediately after the restricted-entry interval statement:

> "Exception: if the product is soil-injected or soil-incorporated, the Worker Protection Standard, under certain circumstances, allows workers to enter the treated area if there will be no contact with anything that has been treated."

In the initial period after the WPS was issued and while guidance was being developed for its implementation, there was confusion about the "no-contact exception" as related to soil-incorporated pesticides. Some individuals mistakenly interpreted the exception as permitting the issuance of no restricted-entry interval for such pesticides. However, when EPA issued a PR Notice in 1995 that permitted the establishment of 4-hour restricted-entry intervals for certain low risk pesticides, it reiterated the principle that all pesticides within the scope of the WPS must have a restricted-entry interval. It also stated that REIs need to be established for three basic reasons: to substitute for the "sprays have dried and dusts have settled" label statement, to incorporate a margin of safety for unknown adverse effects, and the agency cannot anticipate every postapplication activity that may occur. In developing the conditions that must be met for a pesticide to qualify as a low risk (and a 4-hour REI), organophosphates and n-methyl carbamates were specifically excluded due to their inherent toxicity.

During reregistration of phostebupirim, EPA has reevaluated potential postapplication exposures and risks following soil-incorporated applications during planting of corn. It was determined that the Worker Protection Standard and current Agency policy indicate that a restricted-entry interval must be established for this use pattern. The Agency notes that phostebupirim does not qualify as a low risk pesticide, because of its high acute toxicity and because it is classified as an organophosphate. Therefore, the restricted-entry interval will be established based on available data on its dermal toxicity and its skin and eye irritation potential.

Under the Worker Protection Standard (WPS), restricted entry intervals for all uses within the scope of the WPS are based on the acute toxicity of the active ingredient. The toxicity categories of the active ingredient for acute dermal toxicity, eye irritation, and skin irritation are used to determine the WPS REI. If one or more of the three acute toxic affects are in toxicity category I, the WPS REI is established at 48 hours (72 hours in areas that receive less than 25 inches of rainfall per year). Since phostebupirim has a toxicity category of 1 for acute dermal, HED recommends that the REI be changed to 48 hours (72 hours in areas that receive less than 25 inches of rainfall per year), to comply with the Worker Protection Standard.

Data Gaps

The following data are needed to further assess phostebupirim:

- a mixer/loader study to determine exposure from using a closed granular loading engineering control system such as a Smart Box® system

- an applicator exposure study using an enclosed cab.

References

1) Phostebupirim labels.

2) Robbins, Steve. HED Risk Assessment for Use of Aztec 2.1% Granular in/on Corn. February 16, 1995.

3) Tarplee, Brenda. Organophosphates: Evaluation of the Dermal Absorption Factor - Report of the Hazard Identification Assessment Review Committee. February 24, 1999.

4) Pettigrew, Hugh M. and John E. Walan. Route to Route Extrapolation. October 9, 1998.

5) HED Science Advisory Council for Exposure, Policy.007, "Use of Values from the PHED Surrogate Table and Chemical-Specific Data." Health Effects Division, Office of Pesticide Programs, January 1999.

6) PHED Surrogate Exposure Guide. Health Effects Division, Office of Pesticide Program, August 1998.

7) Corn Insecticide Cluster Risk Assessment for Occupational Exposure. November 1993.

8) Tice, John. Requested Waiver of WPS Label Statements for Aztec 2.1% Granular Insecticide. September 13, 1994. DP Barcode D204309.